

Organization **CLIOU** **BLAUGREEN**

United States Patent and Trademark Office

P.O. Box 1450

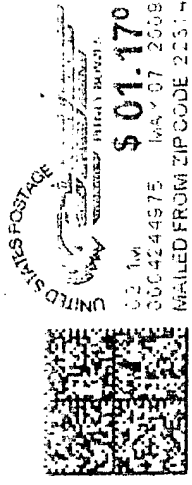
Alexandria, VA 22313-1450

If Undeliverable Return in Ten Days

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

AN EQUAL OPPORTUNITY EMPLOYER





UNITED STATES PATENT AND TRADEMARK OFFICE



UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/888,304 | 06/22/2001 | Robert K. Evans | 20703Y | 9551 |

210 7590 05/07/2009
MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

| |
|----------|
| EXAMINER |
|----------|

WEHBE, ANNE MARIE SABRINA

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1633

| | |
|-----------|---------------|
| MAIL DATE | DELIVERY MODE |
|-----------|---------------|

05/07/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/888,304 | EVANS, ROBERT K. | |
| | Examiner | Art Unit | |
| | Anne Marie S. Wehbe | 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 21-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 21-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/12/09 has been entered. Applicant's request for consideration of the after-final amendment filed on 1/12/09 is acknowledged. Please note that the after-final claim listing was previously entered, see the Advisory action mailed on 2/26/09. Claims 14-20 are canceled and claims 1-13 and 21-26 are currently pending and under examination in the instant application. An action on the merits follows.

Claim Rejections - 35 USC § 103

The rejection of claims 1-13, and 21-26 under 35 U.S.C. 103(a) as being unpatentable over WO 96/04932 (1996), hereafter referred to as Balasubramanian et al., in view of WO 97/25072 (1997), hereafter referred to as Engler et al., is maintained. No claims have been amended, added, or canceled. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below. It is also noted that applicant's arguments were previously considered in the Advisory action mailed on 2/26/09.

The applicant reiterates their argument that Engler et al. teaches away from combining a cationic surfactant with a high molecular weight block copolymer such as CRL-1005 by showing that neither benzalkonium chloride nor cetylpyridium enhanced gene transfer. In their opinion the data in Example 5 of Engler is not conclusive since no negative control data was presented, and accordingly, the applicant concludes that the skilled artisan viewing the Engler data would not find that cationic detergents and some of the nonionic detergents had any effect on gene transfer.

In response, it is first noted that the claims under examination are product claims, not method claims for enhancing gene transfer. Second, as discussed in previous office actions, Engler was cited to supplement Balasubramanian et al. by teaching that cationic detergents, a class of surfactants, can be included in a composition for gene delivery resulting in the delivery of nucleic acids to cells (Engler et al., pages 4-5, and 20-21). In the working examples on pages 14-15, Engler et al. demonstrates that while some surfactants improve gene transfer more than others, Engler et al. clearly shows positive gene transfer using DNA in the form of recombinant adenoviral vector and cationic surfactants. Applicant's contention that the lack of negative control invalidates these results is not agreed. Neither is it agreed that the use of a "+" in the result column for gene transfer and expression would be interpreted by a skilled artisan as background staining. The specification indicates that the "+" represents minimal staining, not background or negative staining. While it may be agreed that the "<+" staining observed for the cationic detergent benzalkonium chloride might be considered a negative result, the "+" staining observed using the cationic detergent cetylpyridium appears to indicate gene transfer and expression absent any concrete evidence to the contrary. The fact that some other detergents

Art Unit: 1633

results in "+++" staining also does not teach away from the use of a cationic detergent- "[a] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Further, the office maintains that Engler et al. makes the clear statement that cationic detergents/surfactants can be used to enhance gene delivery. The fact that Engler lists more than one reagent capable of having this effect does not "teach away" from the inclusion of cationic detergents in a gene delivery composition. As such, applicant's argument that Engler et al. teaches away from using cationic detergents is not found persuasive.

Further, as indicated above, the instant claims are product claims, not methods claim for using the product to enhance gene delivery or improve expression of a transgene. The claimed product elements are obviated by the combined teachings of Balasubramanian et al., who teaches the combination of polynucleotide vaccines, a nonionic surfactant, and an adjuvant comprising a high molecular weight nonionic polyoxyethylene/ polyoxypropylene block copolymers of the general formula $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b(\text{C}_2\text{H}_4\text{O})_a\text{H}$, such as CRL-1005, and Engler et al. who teaches that cationic surfactants can be added to DNA delivery systems resulting in gene transfer. Further, based on the demonstration by Engler et al. that a formulation comprising a recombinant adenoviral vector and a cationic surfactant such as cetylpyridium can be delivered to cells resulting in detectable gene expression, the skilled artisan would have predicted that a combination as claimed, comprising an adjuvant comprising a high molecular weight nonionic polyoxyethylene/ polyoxypropylene block copolymers of the general formula $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b(\text{C}_2\text{H}_4\text{O})_a\text{H}$, such as CRL-1005, a polynucleotide DNA vaccine, a nonionic surfactant, and a cationic surfactant would be capable of being delivered to cells with the result

Art Unit: 1633

of gene expression. A demonstration of “enhanced” gene delivery is not required to obviate the claimed compositions as this property is not a claimed limitation.

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not

Art Unit: 1633

available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/

Primary Examiner, A.U. 1633